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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,734	10/06/2000	Ib Mendel-Hartvig	10806-129	1611

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/582,734	MENDEL-HARTVIG ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed December 15, 2003 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4 and 6-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, part (A) the recitation "adapted" is vague and indefinite. It is unclear how the application zone is adapted for application of liquid.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3, 7, 9, 10, 13, 14, 18, 20, 21, 24, 25, 27, 28 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Dafforn et al (US 4,981,786).

Dafforn et al disclose an immunoassay device and method for determining an analyte in a sample. Dafforn et al also disclose that the device comprises a bibulous material which is susceptible to traversal by an aqueous medium in response to capillary force (flow matrix), (col 7, lines 8-10). Dafforn et al disclose that the device

may be used in assays wherein absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 10-16). Dafforn et al disclose the device comprises a first means for introducing a sample into the device and second means other than the first means for introducing a liquid reagent other than the sample into the device (col 3, lines1-20). Dafforn et al disclose that the liquid reagent can be an ancillary reagent such as a buffer or a labeled reagent (Reactant*). Dafforn et al disclose that the labeled reagent can be provided as liquid reagent or predeposited (col 19, line 15 – col 20, line 22). Dafforn et al disclose that the liquid reagent can be added upstream of the test solution (sample) (col 18, lines 27-29). Dafforn et al also disclose that both of these application zones are located upstream of a immunosorbing zone (detection zone) and that specific binding members (antibodies) (Reactant I) are immobilized in the immunosorbing zone (col 18, line 3 – col 19, line 48). Dafforn et al disclose that the strip may be coated with a material (col 19, lines 1-9). Dafforn et al disclose that the device contains dividers (spacers) between the first means and second means. Dafforn et al also disclose that the sample may be introduced before the liquid reagent if so desired (col 18, lines 20-32). Dafforn et al disclose that the contact portion can also serve as the immunosorbing zone (detection zone) or separate immunosorbing zones can be utilized depending on the particular assay protocol chosen (col 18, lines 45-48). Dafforn et al also disclose that the application of liquid can be performed simultaneously in the application zones (col 24,

lines 30-32). Dafforn et al also disclose that the reagents can be predeposited in the matrix. Dafforn et al also disclose packaging the components into a kit.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 2, 4, 6, 8, 11, 19, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al (US 4,981,786).

See above for teachings of Dafforn et al.

Dafforn et al differ from the instant invention in failing to specifically teach n">n' wherein Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix.

Dafforn et al is silent with respect to substantially simultaneously adding Reactant*, upstream of liquid application zone for sample. However, Dafforn et al specifically teach that the Reactant* can be applied upstream of the liquid application zone for sample. Dafforn et al also disclose many embodiments regarding Reactant* in which Reactant* is applied upstream of the application zone of sample or to the same zone as the sample. Although, Dafforn teaches that when (Reactant*) is added upstream of sample, that the liquid reagent usually is added following the addition of sample (col 13, lines 32-44), Dafforn also teaches the addition of liquid reagents simultaneously (col 24). Therefore, it would have been obvious to one of ordinary skill in the art to add Reactant* upstream of a liquid application zone for sample and to apply the liquids simultaneously in order to optimize assay conditions. Further, it is well settled that a reference must be evaluated for all disclosures not just its preferred embodiments. *In re Mills,* 470 F. 2d 649, 176 USPQ 196 (CCPA 1972).

9. Claims 12, 15, 16, 26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al in view of Robinson et al (WO 95/16914).

See above for teachings of Dafforn et al.

Dafforn et al differ from the instant invention in failing to specifically teach n">n' wherein Reactant*, is upstream of a liquid application zone for sample and the liquids are applied substantially simultaneously to the flow matrix.

Robinson et al disclose the use of calibration zone(s), in which a calibration reagent is immobilized and has biospecific affinity for the analyte of interest or the binding partner of interest (page 15, lines 15-24). Robinson et al also disclose a releasable reagent predeposited (abstract). Robinson et al also disclose that the device may be a flow through device such as test strip (page 5, lines 7-22). Robinson et al also disclose that the specific binding partner can be coupled to or conjugated to the calibrator (see page 17), to form a complex for detection. Robinson et al disclose that the reagents may be antigen/antibody complexes. Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-16) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed (page 14, lines 24-26).

It would have been obvious to one of ordinary skill in the art to incorporate the use of a calibrator zone as taught by Robinson et al into the method and device of Dafforn et al because Robinson et al disclose that calibrator zones used in this manner offers means for calibrating the assay as part of the assay procedure (page 3, lines 15-16) and also provides advantages for additional compensation for various factors in the assay system which may influence the level of signal observed.

10. Claims 17 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al in view of Self et al (US 4,446,231).

See above for teachings of Dafforn et al.

Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune diseases. Self et al shows that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances.

It would have been obvious to one of ordinary skill in the art to use immunoassays as taught by Self et al for the diagnosis of autoimmune diseases because Self et al shows that immunoassays are used for the detection and/or determination of autoimmune diseases and that immunoassays have a wide application, in both clinical and non-clinical fields and that they are particularly useful in any circumstance where it is necessary to detect and/or determine small or very small amounts of substances. Therefore it would have been obvious to one of ordinary skill in the art to use the device and method of Dafforn et al for diagnosing autoimmune disease.

11. Claims 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dafforn et al in view of Goerlach-Graw et al (US 5,556,789).

See above for teachings of Dafforn et al.

Dafforn et al differ from the instant invention in failing to specifically teach wherein each spacer comprises a strip attached to the flow matrix.

Goerlach-Graw et al disclose barriers in the form of strips in a flow matrix. Goerlach-Graw et al disclose that such barriers can be integrated at any desired position between the sample application zone and the reagent zone (col 6). Goerlach-Graw et al disclose that these barriers provide for a device wherein flooding of the test elements with sample liquid is avoided by using these retardation zones.

It would have been obvious to one of ordinary skill in the art to incorporate barriers such as taught by Goerlach-Graw et al into the device and method of Dafforn et al because Goerlach-Graw et al shows that these barriers provide for a device wherein flooding of the test elements with sample liquid is avoided by using these retardation zones.

Response to Arguments

12. Applicant's arguments filed December 15, 2003 have been fully considered but they are not persuasive.

Applicant argues that Dafforn does not teach or suggest a method or device wherein flow is initiated by adding liquid to each zone in such a way that $liquid_{n+1}$ contacts the flow matrix substantially simultaneously with and is transported through the matrix immediately after $liquid_n$, added to the nearest downstream application zone LZ_n.. Applicant directs Examiner's attention to column 24, lines 29-37 which states that "The assay can be conducted by adding a sample suspected of containing HCG at the first opening and simultaneously adding a developer solution containing enzyme substrate at the second opening. During subsequent incubation, HCG bind to the conjugate, the complex carried by the moving developer to the detection zone where it binds, and the

bound complex acts on the substrate to produce color at the detection zone when HCG is present in the sample". Applicant contends that Dafforn et al teach that "during subsequent incubation, HCG binds to the conjugate, the complex is carried by the moving developer to the detection zone" (col 24, lines 33-24) and thus, Dafforn et al teach that the HCG-enzyme conjugate complex mixes with the developer prior to arrival of the HCG in the detection zone. This is not found persuasive because it appears that Applicant is trying to assert that two separate liquid fronts are moving toward the detection zone, one containing analyte (i.e. sample), and the other containing the labeled reagent. And that a complex between the analyte and the labeled reagent is not formed prior to both liquid-fronts reaching the detection zone. If this is a correct interpretation of the argument, it is not found persuasive because it is not on point. The claims are not limited to a method where the labeled reagent is moving in a separate front, i.e. behind a sample liquid. Instead, the claims recite an embodiment where the labeled reactant is located in the same zone where sample is added, (i.e. $LZ_{n"}R^*$ and LZ_n with n" $\geq$ n'), since n is recited as the position of the application zone (LZ_n), the indication that n" is $\geq$ n' is interpreted as an embodiment where the sample application zone and the zone for the labeled reactant is the same, i.e. Dafforn, column 24, lines 23-46. In this case, a complex between the analyte and the labeled reactant is formed when sample is added to LZ_n, and this complex is moving in front of any liquid that is added to the other liquid addition zones. Because the claims do not make clear what "liquid" may be added to the various zones, this "liquid" could be buffer or substrate solution, in which case, after the complex of Dafforn reaches the detection zone, the

bound complex acts on any substrate solution that subsequently enters the detection zone, resulting in a color change. These teachings are seen to be the same as those of the instant claims.

With respect to Applicants arguments that the complex mixes with the developer prior to arrival of the HCG in the detection zone This is not found persuasive because regardless if the developer is added or not the complex will flow toward the detection zone. Furthermore, there is simply no support for the Applicant's assertion that the complex and developer mix. The addition of developer after the complex would flow behind the complex. Further, as disclosed by Dafforn absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 12-16). Therefore, when sample is applied to application zone downstream of liquid reagent, the sample begins to migrate and therefore even when the sample and liquid reagent are added simultaneously the sample would flow in front of liquid reagent. If the complex and developer were mixed together the reaction would occur before the detection zone. Dafforn clearly states (col 24, lines 35-37) that the reaction occurs at the detection zone. Therefore, the complex binds to the immobilized antibody and then the developer reacts to produce a color change. Thus, Dafforn reads on the instantly recited claims.

Applicant argues that Dafforn does not teach or suggest the flow matrix comprises liquid application zones having zone spacers there between, i.e., in the flow matrix, rather than in a housing well. This is not found persuasive because instantly

recited claims 10 and 24 merely recite wherein the zones $LZ_m..LZ_n..LZ_1$ have zone spacers between each other. One skilled in the art would recognize that the dividers of Dafforn et al are incorporated as part of the flow matrix between the application zones and thus would act as spacers. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted tha thee features upon which applicant relies (i.e., in the flow matrix, rather than in a housing well) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns,* 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, Dafforn reads on the instantly recited claims.

Applicants argue that Dafforn et al does not teach or suggest an additional zone $LZ_n..R$ as presently claimed, relating to calibration, particularly, integral with their device, or relating to a calibration zone in their device, calibrator predeposited in or applied to a matrix, or a binder for a calibrator in a calibration zone. This is not found persuasive because Examiner has not relied upon Dafforn et al for these teachings but rather has relied upon Robinson et al for these teachings and there advantages. Further, Robinson et al clearly disclose (page 5, lines 7-15) that the device can be a test strip (same as Daddorn) and robinson clearly states the advantages of using calibration zones and calibration reagents (page 3, lines 15-16 and page 14, lines 24-26). Therefore, it is the Examiner's position that the combination of Dafforn et al and Robinson et al is proper and thus the rejection is maintained.

Applicants argue that the deficiencies of Dafforn et al are not resolved by Self. That is, while Self discloses an immunoassay using an amplified cyclic detection system, Applicants find no teaching or suggestion by Self relating to a method or device for dtermination of an anlyte in a sample and a flow matrix employing a combination of biospecific affinity reactants and liquid application zones and flow as defined in claims 1 and 18. This is not found persuasive Examiner has not relied upon Self for these limitations but rather has relied upon Dafforn et al for these limitations. Further, Dafforn et al specifically teach that the device may be utilized in any number of assay wherein absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 11-16). Further, Dafforn et al disclose that the device can be used to detect autoimmune antibodies and antibodies to allergens (col 5, lines 1-6). Since, Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune disease. It is the Examiner's position that it would have been obvious to one of ordinary skill in the art to combine the teachings of Dafforn et al and Self et al.

Conclusion

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
February 17, 2004

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